STN/East Search Strategy attachment #17

(FILE 'HOME' ENTERED AT 12:30:55 ON 13 JUL 2001)

FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 12:32:11 ON 13 JUL 2001

L1 28231 S LUCIFERASE
L2 301 S L1 AND RENILLA
L3 3 S L2 AND (CLEAV? (5N) PROTEASE)
L4 3 DUP REM L3 (0 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 12:34:44 ON 13 JUL 2001

L5 0 S L2 AND PROTEASE
L6 0 S L2 AND PROTEA?

FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 12:35:57 ON 13 JUL 2001

L7 5 S L2 AND PROTEASE
L8 5 DUP REM L7 (0 DUPLICATES REMOVED)
L9 16 S L1 AND (CLEAV? (5N) PROTEASE)

FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 12:38:48 ON 13 JUL 2001

L10 10 DUP REM L9 (6 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 12:40:56 ON 13 JUL 2001

L11 0 S CASPASE-3

FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 13:36:27 ON 13 JUL 2001

L12 9291 S CASPASE-3
L13 1 S L2 AND (RECOGNITION (2N) SEQUENCE)
L14 0 S L2 AND DEVD
L15 1 S L2 AND (RECOGNITION (2N) SITE)
L16 3 S L2 AND (CLEAVAGE (2N) SITE)
L17 54 S L12 AND (RECOGNITION (2N) (SEQUENCE OR SITE))
L18 24 DUP REM L17 (30 DUPLICATES REMOVED)
L19 1304 S L12 AND DEVD
L20 900 S L12 (10N) DEVD
L21 32 S L20 AND (CLEAVAGE (2N) SITE)
L22 14 DUP REM L21 (18 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 13:43:20 ON 13 JUL 2001

FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 13:46:30 ON 13 JUL 2001

L23 3539 S CASPASE-6 OR CASPASE-8 OR CASPASE-9
L24 67 S L23 AND (VEHD OR LETD OR LEHD)
L25 31 DUP REM L24 (36 DUPLICATES REMOVED)
L26 8 S L25 AND CLEAVAGE

FILE 'STNGUIDE' ENTERED AT 13:48:42 ON 13 JUL 2001

L27 0 S CASPASE AND LUCIFERASE

FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 13:55:44 ON 13 JUL 2001

L28 51 S CASPASE AND LUCIFERASE
L29 32 DUP REM L28 (19 DUPLICATES REMOVED)

FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 10:55:57 ON 17 JUL

```
     2001
L1         28267 S LUCIFERASE
L2           589 S RENILLA
L3           249 S L1 (5N) L2
L4             1 S L3 AND REINFORMIS
L5           100 S L3 AND RENIFORMIS
L6            60 DUP REM L5 (40 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 10:58:10 ON 17 JUL 2001

     FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 10:58:44 ON 17 JUL
     2001

=> l6 and catalytic
L6 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l6 and catalytic
L7             0 L6 AND CATALYTIC

=> s l6 and activ?
L8            28 L6 AND ACTIV?

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9             28 DUP REM L8 (0 DUPLICATES REMOVED)
```

(FILE 'HOME' ENTERED AT 12:30:55 ON 13 JUL 2001)

FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 12:32:11 ON 13 JUL 2001

L1 28231 S LUCIFERASE
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L5 0 S L2 AND PROTEASE
L6 0 S L2 AND PROTEA?

FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 12:35:57 ON 13 JUL 2001

L7 5 S L2 AND PROTEASE
L8 5 DUP REM L7 (0 DUPLICATES REMOVED)
L9 16 S L1 AND (CLEAV? (5N) PROTEASE)

FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 12:38:48 ON 13 JUL 2001

L10 10 DUP REM L9 (6 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 12:40:56 ON 13 JUL 2001

L11 0 S CASPASE-3

FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 13:36:27 ON 13 JUL 2001

L12 9291 S CASPASE-3
L13 1 S L2 AND (RECOGNITION (2N) SEQUENCE)
L14 0 S L2 AND DEVD
L15 1 S L2 AND (RECOGNITION (2N) SITE)
L16 3 S L2 AND (CLEAVAGE (2N) SITE)
L17 54 S L12 AND (RECOGNITION (2N) (SEQUENCE OR SITE))
L18 24 DUP REM L17 (30 DUPLICATES REMOVED)
L19 1304 S L12 AND DEVD
L20 900 S L12 (10N) DEVD
L21 32 S L20 AND (CLEAVAGE (2N) SITE)
L22 14 DUP REM L21 (18 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 13:43:20 ON 13 JUL 2001

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L23 3539 S CASPASE-6 OR CASPASE-8 OR CASPASE-9
L24 67 S L23 AND (VEHD OR LETD OR LEHD)
L25 31 DUP REM L24 (36 DUPLICATES REMOVED)
L26 8 S L25 AND CLEAVAGE

FILE 'STNGUIDE' ENTERED AT 13:48:42 ON 13 JUL 2001

L9 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2001 ACS
AN 2000:241540 CAPLUS
DN 132:290498
TI Cloning, expression and sequences of wild-type and modified forms of secreted **Renilla luciferase** and their use as reporter proteins
IN Escher, Alan P.; Liu, Jingxue
PA Loma Linda University, USA
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000020619	A2	20000413	WO 1999-US20093	19990902
	WO 2000020619	A3	20000706		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6228604	B1	20010508	US 1999-330317	19990610
PRAI	US 1998-99214	P	19980904		
	US 1999-330317	A	19990610		
	US 1996-629822	B2	19960410		
	US 1996-682080	A2	19960715		
	US 1996-695191	A2	19960807		
	US 1998-152031	B2	19980911		

AB A DNA and encoded amino acid sequences of a secreted functional form of wild type **Renilla luciferase** are disclosed. Cloning and expression of the secreted **Renilla luciferase** are described. Bioluminescence assays of luciferase **activity** in culture media contg. secreted **Renilla luciferase** and in cell lysates of transfected mammalian cells are described. Cloning and expression of substitution mutants of the the secreted **Renilla luciferase** are also disclosed and their sequences are provided. The wild-type and modified forms of the secreted **Renilla luciferase** could be used as reporter proteins in biol. assays. Use of the mutant secreted **Renilla luciferase** and Seap protein in dual reporter system is also disclosed. Also, a stable mammalian packaging cell line which produces retroviruses carrying a polynucleotide encoding a secreted **Renilla luciferase** is described.

EP 1115886 00/20619
WO

L9 ANSWER 19 OF 28 CAPLUS COPYRIGHT 2001 ACS
AN 1994:318319 CAPLUS
DN 120:318319
TI Cloning and expressions of the gene for **luciferase** of **Renilla**
IN Cormier, Milton J.; Lorenz, William W.
PA University of Georgia Res. Found., Inc. Boyd Graduate Studies Res. Cen., USA
SO U.S., 19 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5292658	A	19940308	US 1993-79700	19930617
	US 5418155	A	19950523	US 1993-167650	19931214
PRAI	US 1989-458952		19891229		
	US 1992-933017		19920820		
	US 1993-79700		19930617		

AB A cDNA encoding the **luciferase** of the marine coelenterate **Renilla** has been isolated and characterized. The cDNA can be used for manuf. of the enzyme for use as a label in bioluminescence assays or can itself be directly used to identify luciferase genes from related organisms. Amino acid sequence-derived probes were used to screen a Renilla **reniformis** cDNA bank in .lambda.gt11. The cDNA was cloned into the com. expression vector pTZ18R for manuf. of the enzyme in Escherichia coli. The protein was purified chromatog. 6.3-fold (5.9% yield) from lysates of E. coli to give an enzyme with a specific **activity** of .apprx.1.8.times.1015 h.nu. sec-1mg-1.

L9 ANSWER 10 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1999:483360 BIOSIS
DN PREV199900483360
TI Improved assay sensitivity of an engineered secreted **Renilla luciferase**.
AU Liu, Jingxue; Escher, Alan (1)
CS (1) Center for Molecular Biology and Gene Therapy and Department of Microbiology and Molecular Genetics, Loma Linda University, Loma Linda, CA USA
SO Gene (Amsterdam), (Sept. 3, 1999) Vol. 237, No. 1, pp. 153-159. ISSN: 0378-1119.
DT Article
LA English
SL English
AB We have previously reported the construction of a functional **Renilla luciferase** enzyme secreted by mammalian cells when fused to the signal peptide of human interleukin-2. The presence of three predicted cysteine residues in the amino acid sequence of **Renilla luciferase** suggested that its secreted form could contain oxidized sulfhydryls, which might impair enzyme **activity**. In this work, four secreted **Renilla luciferase** mutants were constructed to investigate this possibility: three luciferase mutants in which a different cysteine residue was replaced by an alanine residue, and one luciferase mutant in which all three cysteine residues were replaced by alanine residues. Simian cells were transfected with the genes encoding these mutant luciferases, as well as with the original gene construct, and cell culture media were assayed for bioluminescence **activity**. Only media containing a mutated luciferase with a cysteine to alanine substitution at position 152 in the preprotein showed a marked increase in bioluminescence **activity** when compared to media containing the original secreted **Renilla luciferase**. This increase in light emission was due in part to enhanced stability of the mutant enzyme. This new enzyme represents a significant improvement in the sensitivity of the secreted **Renilla luciferase** assay for monitoring gene expression.

L22 ANSWER 10 OF 14 MEDLINE DUPLICATE 6
AN 1999138716 MEDLINE
DN 99138716 PubMed ID: 9973322
TI Caspase-mediated cleavage of APC results in an amino-terminal fragment with an intact armadillo repeat domain.
AU Webb S J; Nicholson D; Bubb V J; Wyllie A H
CS Department of Pathology, University Medical School, Edinburgh, EH8 9AG, UK.. sjwebb01@homer.louisville.edu
SO FASEB JOURNAL, (1999 Feb) 13 (2) 339-46.
Journal code: FAS; 8804484. ISSN: 0892-6638.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199903
ED Entered STN: 19990413
Last Updated on STN: 19990413
Entered Medline: 19990331
AB During the effector phase of apoptosis, caspase activation appears to be responsible for the distinctive structural changes of apoptosis and perhaps for some of the changes in function of the doomed cells. There is therefore interest in identifying caspase substrates and the details of the cleavage events. Here we define precisely the event responsible for generation of a stable 90 kDa fragment from the oncosuppressor protein adenomatous polyposis coli (APC). Using synthetic radiolabeled APC peptides as substrate, we demonstrate cleavage by cytosolic extracts from preapoptotic cells. This cleavage was reproduced by recombinant **caspase-3** and blocked by a tetrapeptide inhibitor Ac-**DEVD**-CHO, which is specific for **caspase-3** family members. Inhibitors specific for caspase-1 and -8 however, were less effective in blocking APC cleavage. Mutation of a candidate DNID caspase-3 target **site** completely abolished **cleavage**. This cleavage may be of biological importance since the 90 kDa fragment consists of a sequence that is highly conserved in the human, rat, mouse, Xenopus, and Drosophila APC, although wide sequence divergence is observed in Drosophila immediately carboxy-terminal to the DNID **site**. Furthermore, **cleavage** at this **site** separates two significant functional domains: an amino-terminal armadillo repeat and an adjacent series of beta-catenin binding sites. Further circumstantial evidence for the significance of APC-related pathways in apoptosis is provided by the observation that apoptosis also induces cleavage of beta-catenin itself, a protein known to accumulate in cells depleted in functional APC and that appears to link cell-cell signaling to changes in transcription and cell movement.

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS
AN 2001:473045 CAPLUS
TI A bioluminescence resonance energy transfer (BRET) fusion molecule and method of use
IN Joly, Erik
PA Biosignal Packard Inc., Can.
SO PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001046694	A2	20010628	WO 2000-CA1513	20001222

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI CA 1999-2292036 A 19991222
AB This invention provides a bioluminescence resonance energy transfer (BRET) fusion mol., and method of use. The fusion mol. comprises three components: a bioluminescent donor protein (BDP), a modulator, and a fluorescent acceptor mol. (FAM), wherein the FAM can accept energy from the BDP-generated luminescence when these components are in an appropriate spatial relationship and in the presence of an appropriate substrate. The modulator can either influence the proximity/orientation of the BDP and the FAM and thereby the energy transfer between these components, or it can play a different role in affecting the energy transfer between the BDP-generated activated product and the FAM. The fusion protein, Rluc:PKA:EYFP (contg. **Renilla luciferase** fusion protein with a synthetic peptide contg. a phosphorylation site for protein kinase A fusion protein with enhanced yellow fluorescent protein), was recombinantly prepd. and used in a BRET assay with coelenterazine h deriv. (as luminescent substrate). The BRET ratio was forskolin dose-dependent such that the BRET ratio decreased with an increase in the concn. of forskolin.

L4 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:245219 BIOSIS
DN PREV200100245219
TI BRET2 (bioluminescence resonance energy transfer) monitoring of betaarrestin recruitment to agonist-stimulated GPCRs.
AU Houle, Benoit (1); Joly, Erik (1); Caron, Mireille (1); Angers, Stephane; Bouvier, Michel; Menard, Luc (1)
CS (1) BioSignal Packard Inc., 1744 William, Montreal, Quebec, H3J 1R4 Canada
SO FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A219. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001

ISSN: 0892-6638.
DT Conference
LA English
SL English
AB Bioluminescence resonance energy transfer (BRET) is a non-radiative energy transfer which takes place between a donnor (a **luciferase**) and an acceptor (a green fluorescent protein, GFP) in close proximity, upon addition of the substrate for the **luciferase**. We have developed an improved BRET system, BRET2, which uses the **Renilla luciferase** (Rluc) as the donnor and the coelenterazine derivative DeepBlueCTM as the substrate, resulting in much better separation between the **luciferase** and GFP emissions. Since DeepBlueCTM is cell permeant, BRET2 allows the design of various live-cell assays to monitor protein-protein interactions. For example, we have successfully designed assays that permit detection of protease activity (e.g. caspase 3) using a fusion protein bearing a specific **protease cleavage** site between the Rluc and GFP coding sequences. Upon activation of the **protease**, the fusion protein is **cleaved**, leading to a decrease in the BRET signal. BRET2 can also be used to monitor the induction of protein interactions. In such assays, the donor and acceptor are fused to proteins of interest, known to interact. Using this approach we have designed assays aimed at detecting activation of G protein-coupled receptors (GPCRs) by agonists. This assay is based on the observation that activation of the majority of GPCRs by agonist ligands leads to the recruitment of betaarrestin (a protein that is involved in receptor desensitization and sequestration) to the receptor. Using the beta2 adrenergic receptor (beta2AR) fused to Rluc, we showed that the agonist isoproterenol induced recruitment of the fusion protein betaarrestin-GFP in a dose-dependent fashion, and that this response could be blocked by antagonists. A similar assay using the vasopressin receptor 2-Rluc fusion demonstrated a vasopressin-dependent BRET response with and observed EC50 of 3.7 nM. These data show that the BRET2/arrestin assay could be used as a general tool to detect GPCR activation by ligands, and could be applied to ligand identification for orphan receptors.

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2001 ACS
AN 1998:255495 CAPLUS
DN 129:51174
TI Cleavage of cellular proteins by the HIV-1 protease
AU Korant, Bruce D.; Rizzo, Christopher J.; Lu, Zichun; Strack, Peter; Frey, Michelle W.
CS DuPont Merck Pharmaceutical Co., Experimental Station, Wilmington, DE, 19880-0336, USA
SO Biomed. Health Res. (1997), 13(Proteolysis in Cell Functions), 520-523
CODEN: BIHREN; ISSN: 0929-6743
PB IOS Press
DT Journal
LA English
AB Cleavage of non-viral proteins is rarely obsd. with the HIV-1 protease (HIV pr). One such cleavage event occurs with **Renilla luciferase**, inactivating the light-producing ability of the latter enzyme. This result can be incorporated into a rapid, sensitive and quant. assay for HIV pr activity. Another cell protein hydrolyzed by HIV pr is bcl-2, a cytoprotective protein. This cleavage event has important biol. consequences, leading to enhanced HIV replication and programmed death of the host cell. A strategy is proposed to suppress HIV with

non-cleavable mutants of bcl-2.